

PATENT  
Attorney Docket No.: 015389-002640US  
Client Reference No.: 018/213C



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Thomas R. Cech et al.

Application No.: To Be Assigned

Filed: Herewith

For: HUMAN TELOMERASE  
CATALYTIC SUBUNIT: DIAGNOSTIC  
AND THERAPEUTIC METHODS

Examiner: To Be Assigned

Art Unit: To Be Assigned

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

#7

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 08/912,951, filed August 14, 1997 (Attorney Docket No. 015389-002600US). If the examiner would like additional copies of any of these cited references, applicants will happily provide them.

It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom. As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.


Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the

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Page 2

PATENT

Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Hugh Wang  
Reg. No. 47,163

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: 650-326-2400  
Fax: 650-326-2422  
HW:adm

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Substitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 10

### Complete if Known

Application Number	To Be Assigned
Filing Date	Herewith
First Named Inventor	Cech, Thomas J.
Group Art Unit	To Be Assigned
Examiner Name	To Be Assigned
Attorney Docket Number	015389-002640US

PTO  
263710-01  
01/11/02

### U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	A	08/751,189		Harrington, et al.	11/15/96	
	B	60/038,750		Counter, et al.	02/20/97	
	C	3,817,837		Tanenholtz et al.	06-18-74	
	D	3,850,752		Schuurs et al.	11-26-74	
	E	3,939,350		Kronick et al.	02-17-76	
	F	3,996,345		Ullman et al.	12-01-76	
	G	4,275,149		Litman et al.	06-23-81	
	H	4,277,437		Maggio	07-07-81	
	I	4,366,241		Tom et al.	12-28-82	
	J	4,683,195		Mullis et al.	07-28-87	
	K	4,683,202		Mullis	07-28-87	
	L	4,816,567		Cabilly et al.	03-28-89	
	M	4,965,188		Mullis et al.	10-23-90	
	N	5,489,508		West et al.	02-06-96	
	O	5,583,016		Villeponteau et al.	12-10-96	
	P	5,747,317		Cao	05-05-98	
	Q	5,770,422		Collins	06-23-98	
	R	6,093,809		Cech, et al.	07/25/00	
	S	6,258,535	B1	Villeponteau et al.	07/10/01	
	T	6,261,556	B1	Weinrich et al.	07/17/01	
	U	6,261,836	B1	Cech et al.	07/17/01	

### FOREIGN PATENT DOCUMENTS

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	V	JP	09154575-A			06-17-97		
	W	PCT	WO 84/03564			09-13-84		
	X	PCT	WO 95/13382			05-18-95		
	Y	PCT	WO 96/01835			01-25-96		
	Z	PCT	WO 96/12811			05-02-96		
	AA	PCT	WO 96/19580			06-27-96		

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<sup>1</sup> Unique citation designation number. <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

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	AB	PCT	WO 96/40868			12-19-96		
	AC	PCT	WO 98/01542			01-15-98		
	AD	PCT	WO 98/01543			01-15-98		
	AE	PCT	WO 98/07838			03-05-98		
	AF	PCT	WO 98/08938			02-26-98		
	AG	PCT	WO 98/21343			05-22-98		
	AH	PCT	WO 98/37181			08-27-98		
	AI	PCT	WO 98/45450			10-15-98		
	AJ	PCT	WO98/59040			12/30/98		
	AK	PCT	WO99/01560			01/14/99		

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Sheet	3	of	10
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OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AL	1994 Genome Issue of <i>Science</i> (265:1981f)	
	AM	Anderson and Young, "Quantitative Filter Hybridization" in <i>Nucleic Acid Hybridization</i> pp73-111 (1985)	
	AN	Ausubel <i>et al.</i> , Current Protocols in Molecular Biology, John Wiley & Sons, New York NY (1989)	
	AO	Autexier <i>et al.</i> , "Reconstitution of human telomerase activity and identification of a minimal functional region of the human telomerase RNA," (1996) <i>EMBO J.</i> , 15:5928	
	AP	Auxexier and Greider, "Functional reconstitution of wild-type and mutant <i>Tetrahymena</i> telomerase," (1994) <i>Genes Develop.</i> , 8:563	
	AQ	Berger and Kimmel, <i>Guide to Molecular Cloning Techniques</i> , Meth. Enzymol., vol. 152, Academic Press, San Diego CA (1987)	
	AR	Blessman <i>et al.</i> , "Addition of Telomere-Associated HeT DNA Sequences "Heals" Broken Chromosome Ends in <i>Drosophila</i> ," (1990) <i>Cell</i> , 61:663	
	AS	Bitter <i>et al.</i> , "Expression and secretion vectors for yeast," <i>Meth Enzymol.</i> , (1987) 153:516	
	AT	Blackburn and Chiou, "Non-nucleosomal packaging of a tandemly repeated DNA sequence at termini of extrachromosomal DNA coding for rRNA in <i>Tetrahymena</i> ," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:2263	
	AU	Blackburn and Gall, "A tandemly repeated sequence at the termini of the extrachromosomal ribosomal RNA genes in <i>Tetrahymena</i> ," (1978) <i>J. Mol. Biol.</i> , 120:33	
	AV	Blackburn, "Telomerases," (1992) <i>Ann. Rev. Biochem.</i> , 61:113	
	AW	Bodnar <i>et al.</i> , "Extension of Life-Span by Introduction of Telomerase into Normal Human Cells," (1998) <i>Science</i> , 279:349	
	AX	Bradford, "A Rapid and Sensitive method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding," (1976) <i>Anal. Biochem.</i> , 72:248	
	AY	Braunstein <i>et al.</i> , "Transcriptional silencing in yeast is associated with reduced nucleosome acetylation," (1993) <i>Genes Develop.</i> , 7:592	

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	AZ	Calvio <i>et al.</i> , "Identification of hnRNP P2 as TLS/FUS using electrospray mass spectrometry," (1995) <i>RNA</i> , 1:724	
	BA	Caruthers <i>et al.</i> , "New chemical methods for synthesizing polynucleotides," (1980) <i>Nucleic Acids Res. Symp. Ser.</i> , 215-223	
	BB	Chan and Tye, "Organization of DNA sequences and replication origins at yeast telomeres," (1983) <i>Cell</i> , 33:563	
	BC	Colbere-Garapin <i>et al.</i> , "A new dominant hybrid selective marker for higher eukaryotic cells," (1981) <i>J. Mol. Biol.</i> , 150:1	
	BD	Cole <i>et al.</i> , "The EBV-hybridoma technique and its application to human lung cancer," Monoclonal Antibodies and Cancer Therapy, Alan R. Liss Inc., New York NY 77-96 (1985)	
	BE	Collins <i>et al.</i> , "Purification of Tetrahymena telomerase and cloning of genes encoding the two protein components of the enzyme," (1995) <i>Cell</i> , 81:677	
	BF	Conrad <i>et al.</i> , "RAP1 protein interacts with yeast telomers in vivo: Overproduction alters telomere structure and decreases chromosome stability," (1990) <i>Cell</i> , 63:739	
	BG	Coombs, <i>Dictionary of Biotechnology</i> , Stockton Press, New York NY (1994)	
	BH	Cote <i>et al.</i> , "Generation of human monoclonal antibodies reactive with cellular antigens," (1983) <i>Proc. Natl. Acad. Sci.</i> , 80:2026	
	BI	Counter <i>et al.</i> , "The catalytic subunit of yeast telomerase," (1997) <i>Proc. Natl. Acad. Sci.</i> , 94:9202	
	BJ	Counter <i>et al.</i> , (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:2900	
	BK	Creighton, <i>Proteins, Structures and Molecular Principles</i> , WH Freeman and Co, New York, NY (1983)	
	BL	Dieffenbach and Dveksler, <i>PCR Primer, a Laboratory Manual</i> , Cold Spring Harbor Press, Plainview NY (1995)	

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	BM	Duplaa <i>et al.</i> , "Quantitative analysis of polymerase chain reaction products using biotinylated dUTP incorporation," (1993) <i>Anal. Biochem.</i> , 212:229	
	BN	Fang <i>et al.</i> , "Oxytricha telomere-binding protein: separable DNA-binding and dimerization domains of the $\alpha$ -subunit," <i>Genes Develop.</i> 7:870 (1993) and Gray <i>et al.</i> , (1991) <i>Cell</i> 67:807	
	BO	Feng <i>et al.</i> , "The RNA Component of Human Telomerase," (1995) <i>Science</i> , 269:1236	
	BP	GenBank Accession No. AA281296	
	BQ	Genbank accession no. AA299878	
	BR	Genbank accession no. AA311750	
	BS	Gilley <i>et al.</i> , "Altering specific telomerase RNA template residues affects active site function," (1995) <i>Genes Develop.</i> , 9:2214	
	BT	Gottschling and Cech, "Chromatin Structure of the Molecular Ends of Oxytricha Mononuclear DNA: Phased Nucleosomes and a Telomeric Complex," (1984) <i>Cell</i> , 38:501	
	BU	Gottschling and Zakian, "Telomere proteins: specific recognition and protection of the natural termini of Oxytricha macronuclear DNA," (1986) <i>Cell</i> 47:195	
	BV	Grant <i>et al.</i> , <i>Meth Enzymol.</i> , (1987) 153:516-544	
	BW	Greenwood <i>et al.</i> , "Phylogenetic relationships within the class oligohymenophorea, phylum ciliophora, inferred from the complete small subunit rRNA gene sequences of <i>Colpidium campylum</i> , <i>Glaucoma chattoni</i> , and <i>Opisthionecta heneguyi</i> ," (1991) <i>J. Mol. Evol.</i> , 3:163	
	BX	Greider and Blackburn, "A telomeric sequence in the RNA of Tetrahymena telomerase required for telomere repeat synthesis," (1989) <i>Nature</i> , 337:331	
	BY	Greider and Blackburn, "Identification of a specific telomere terminal transferase activity in Tetrahymena extracts," (1985) <i>Cell</i> , 43:405	

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	BZ	Greider, "Telomerase is processive, " (1991) <i>Mol. Cell. Biol.</i> , 11:4572	
	CA	Greider, "Telomere Length Regulation," (1996) <i>Ann. Rev. Biochem.</i> , 65:337	
	CB	Hampton <i>et al.</i> , <i>Serological Methods a Laboratory Manual</i> , APS Press, St Paul MN (1990)	
	CC	Harrington <i>et al.</i> , "A Mammalian Telomerase-Associated Protein," (1997) <i>Science</i> , 275:973	
	CD	Harrington <i>et al.</i> , "Human telomerase contains evolutionarily conserved catalytic and structural subunits," (1997) <i>Genes Dev.</i> , 11:3109	
	CE	Hartman and Mulligan, "Two dominant-acting selectable markers for gene transfer studies in mammalian cells," (1988) <i>Proc. Natl. Acad. Sci.</i> , 85:8047	
	CF	Henderson and Blackburn, "An overhanging 3' terminus is a conserved feature of telomeres," (1989) <i>Mol. Cell. Biol.</i> , 9:345	
	CG	Horn <i>et al.</i> , "Synthesis of oligonucleotides on cellulose. Part II: design and synthetic strategy to the synthesis of 22 oligodeoxynucleotides coding for gastric inhibitory polypeptide (GIP)," (1980) <i>Nucleic Acids Res. Symp. Ser.</i> , 225-232	
	CH	Hudson <i>et al.</i> , "An STS-based map of the human genome," (1995) <i>Science</i> , 270:1945	
	CI	Huse <i>et al.</i> , "Generation of a large combinatorial library of the immunoglobulin repertoire in phage lambda," (1989) <i>Science</i> , 246:1275	
	CJ	Johnson <i>et al.</i> , (1991) <i>Mol. Cell Biol.</i> 11:1	
	CK	Kilian <i>et al.</i> , "Isolation of a candidate human telomerase catalytic subunit gene, which reveals complex splicing patterns in different cell types," (1997) <i>Hum. Mol. Genet.</i> , 6:2011	
	CL	Kipling and Cooke, "Hypervariable ultra-long telomeres in mice," (1990) <i>Nature</i> 347:400	
	CM	Klobutcher <i>et al.</i> , "All gene-sized DNA molecules in four species of hypotrichs have the same terminal sequence and an unusual 3' terminus," (1981) <i>Proc. Natl. Acad. Sci.</i> , 78:3015	

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	CN	Koehler and Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity," (1975) <i>Nature</i> 256:495	
	CO	Kosbor <i>et al.</i> , "The production of monoclonal antibodies from human lymphocytes," (1983) <i>Immunol. Today</i> 4:72	
	CP	Lamond and Sproat, (1994) "Isolation and Characterization of Ribonucleoprotein Complexes," pp103-140	
	CQ	Lamond <i>et al.</i> , "Probing the structure and function of U2 snRNP with antisense oligonucleotides made of 2'-OMe RNA," (1989) <i>Cell</i> , 58:383	
	CR	Lendvay <i>et al.</i> , "Senescence mutants of <i>Saccharomyces cerevisiae</i> with a defect in telomere replication identify three additional EST genes," (1996) <i>Genetics</i> , 144	
	CS	Lingner <i>et al.</i> , "Purification of telomerase from <i>Euplotes aedeolatus</i> : requirement of a primer 3' overhang," (1996) <i>Proc. Natl. Acad. Sci.</i> , 93:10712	
	CT	Lingner <i>et al.</i> , "Reverse transcriptase motifs in the catalytic subunit of telomerase," (1997) <i>Science</i> , 276:561	
	CU	Lingner <i>et al.</i> , "Telomerase RNAs of different ciliates have a common secondary structure and a permuted template," (1994) <i>Genes Develop.</i> , 8:1984	
	CV	Lingner <i>et al.</i> , "Telomerase and DNA End Replication: No Longer a Lagging Strand Problem?," (1995) <i>Science</i> 269:1533	
	CW	Lowy <i>et al.</i> , "Isolation of transforming DNA: Cloning the hamster apt gene," (1980) <i>Cell</i> , 22:817	
	CX	Lustig and Petes, Identification of yeast mutants with altered telomere structure," (1986) <i>Proc. Natl. Acad. Sci.</i> , 83:1398	
	CY	Maddox <i>et al.</i> , "Elevated serum levels in human pregnancy of a molecule immunochemically similar to eosinophil granule major basic protein," (1983) <i>J. Exp. Med.</i> , 158:1211	
	CZ	Makarov <i>et al.</i> , "Nucleosomal Organization of Telomere-Specific Chromatin in Rat," (1993) <i>Cell</i> , 73:775	
	DA	McEachern and Blackburn, "runaway telomere elongation caused by telomerase RNA gene mutation," (1995) <i>Nature</i> , 376:403	

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Sheet **8** of **10**

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Application Number	To Be Assigned
Filing Date	Herewith
First Named Inventor	Cech, Thomas J.
Group Art Unit	To Be Assigned
Examiner Name	To Be Assigned
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	DB	Melby <i>et al.</i> , "Quantitative measurement of human cytokine gene expression by polymerase chain reaction," (1993) <i>J. Immunol. Meth.</i> , 159:235	
	DC	Merrifield, "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide," (1963) <i>J. Am. Chem. Soc.</i> , 85:2149	
	DD	Meyerson <i>et al.</i> , "hEST2, the Putative Human Telomerase Catalytic Subunit Gene, Is Up-Regulated in Tumor Cells and during Immortalization," (1997) <i>Cell</i> , 90:785	
	DE	Murray, <i>In McGraw Hill Yearbook of Science and Technology</i> , (1992) McGraw Hill, New York NY, pp 191-196	
	DF	Nakamura <i>et al.</i> , "Telomerase Catalytic Subunit Homologs from Fission Yeast and Human," (1997) <i>Science</i> , 277:955	
	DG	Nakayama <i>et al.</i> , "TLP1: A Gene Encoding a Protein Component of Mammalian Telomerase Is a Novel Member of WD Repeats Family," (1997) <i>Cell</i> , 88:875	
	DH	Nielsen <i>et al.</i> , (1993) "Peptide nucleic acids (PNAs): Potential antisense and anti-gene agents," <i>Anticancer Drug Des.</i> , 8:53	
	DI	Oka <i>et al.</i> , "Inverted terminal repeat sequence in the macronuclear DNA of <i>Stylonychia pustulata</i> ," (1980) <i>Gene</i> , 10:301	
	DJ	Olovnikov, "A theory of marginotomy: The incomplete copying of template margin in enzymic synthesis of polynucleotides and biological significance of the phenomenon," (1973) <i>J. Theor. Biol.</i> , 41:181	
	DK	Orlandi <i>et al.</i> , "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction," (1989) <i>Proc. Natl. Acad. Sci.</i> , 86:3833	
	DL	Prescott, "The DNA of ciliated protozoa," (1994) <i>Microbiol. Rev.</i> , 58:233	
	DM	Price, (1993) <i>Blood Rev.</i> , 7:127	
	DN	Rhodes <i>et al.</i> , "Transformation of maize by electroporation of embryos," (1995) <i>Meth. Mol. Biol.</i> , 55:121	
	DO	Roberge <i>et al.</i> , "A strategy for a convergent synthesis of N-linked glycopeptides on a solid support," (1995) <i>Science</i> , 269:202	

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	DP	Romero and Blackburn, "A conserved secondary structure for telomerase RNA, " (1991) <i>Cell</i> , 67:343	
	DQ	Sambrook <i>et al.</i> , <i>Molecular Cloning, A Laboratory Manual</i> , Cold Spring Harbor Press, Plainview NY (1989)	
	DR	Sandell <i>et al.</i> , "Transcription of yeast telomere alleviates telomere position effect without affecting chromosome stability, "(1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12061	
	DS	Sanger <i>et al.</i> , "DNA sequencing with chain-terminating inhibitors," (1977) <i>Proc. Natl. Acad. Sci.</i> , 74:5463	
	DT	Scharf <i>et al.</i> , "Heat stress promoters and transcription factors," (1994) <i>Result Probl. Cell Differ.</i> 20:125	
	DU	Shampay and Blackburn, "Generation of telomere-length heterogeneity in <i>Saccharomyces cerevisiae</i> ," (1988) <i>Proc. Natl. Acad. Sci.</i> , 85:534	
	DV	Sheen and Levis, "Transposition of the LINE-like retrotransposon TART to <i>Drosophila</i> chromosome termini," (1994) <i>Proc. Natl. Acad. Sci.</i> , 91:12510	
	DW	Singer and Gottschling, "TLC1: Template RNA Component of <i>Saccharomyces cerevisiae</i> Telomerase," (1994) <i>Science</i> 266:404	
	DX	Starling <i>et al.</i> , "Extensive telomere repeat arrays in mouse are hypervariable," (1990) <i>Nucleic Acids Res.</i> , 18:6881	
	DY	Swanton <i>et al.</i> , "Arrangement of Coding and Non-coding Sequences in the DNA Molecules Coding for rRNAs in <i>Oxytricha</i> sp.," (1980) <i>Chromosoma</i> 77:203	
	DZ	Tommerup <i>et al.</i> , "Unusual chromatin in human telomeres," (1994) <i>Mol. Cell. Biol.</i> , 14:5777	
	EA	Trask, "Fluorescence in situ hybridization: application in cytogenetics and gene mapping," (1991) <i>Trends Genet.</i> , 7:149	
	EB	Verma <i>et al.</i> , " <i>Human Chromosomes: A Manual of Basic Techniques</i> ," Pergamon Press, New York NY (1988)	
	EC	Watson, "Origin of concatemeric T7 DNA, " (1972) <i>Nature New Biol.</i> , 239:197	

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	ED	Weinrich <i>et al.</i> , "Reconstitution of human telomerase with the template RNA component hTR and the catalytic protein subunit hTRT," (1997) <i>Nat. Genet.</i> , 17(4):498	
	EE	Wellinger <i>et al.</i> , "Origin activation and formation of single-strand TG <sub>1-3</sub> tails occur sequentially in late S phase on a Yeast linear plasmid," (1993) <i>Mol. Cell. Biol.</i> , 13:4057	
	EF	Wellinger <i>et al.</i> , "Saccharomyces Telomeres Acquire Single-Strand TG <sub>1-3</sub> Tails Late in S Phase," (1993) <i>Cell</i> 72:51	
	EG	Whitehead Institute/MIT Center for Genome Research, Genetic Map of the Mouse, Database Release 10, April 28, 1995	
	EH	Wigler <i>et al.</i> , "Transfer of purified herpes virus thymidine kinase gene to cultured mouse cells," (1977) <i>Cell</i> , 11:223	
	EI	Wigler <i>et al.</i> , "Transformation of mammalian cells with an amplifiable dominant-acting gene," (1980) <i>Proc. Natl. Acad. Sci.</i> , 77:3567	
	EJ	Winter and Milstein, "Man-made antibodies," (1991) <i>Nature</i> , 349:293	
	EK	Wright <i>et al.</i> , "Saccharomyces telomeres assume a non-nucleosomal chromatin structure," (1992) <i>Genes Develop.</i> , 6:197	
	EL	Yu <i>et al.</i> , "In vivo alteration of telomere sequences and senescence caused by mutated Tetrahymena telomerase RNAs," (1990) <i>Nature</i> , 344:126	
	EM	Zahler and Prescott, "Telomere terminal transferase activity in the hypotrichous ciliate <i>Oxytricha nova</i> and a model for replication of the ends of linear DNA molecules," (1988) <i>Nucleic Acids Res.</i> , 16:6953	
	EN	Zakian, Telomeres: Beginning to Understand the End," (1995) <i>Science</i> 270:1601	
	EO	Zaug <i>et al.</i> , "Catalysis of RNA Cleavage by a Ribozyme Derived from the Group I Intron of Anabaena Pre-tRNA <sup>Leu</sup> ,"	

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